Human and mouse tissue-engineered small intestine both demonstrate digestive and absorptive function.

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Public Summary:
Short bowel syndrome (SBS) is a devastating condition in which insufficient small intestinal surface area results in malnutrition and dependence on intravenous parenteral nutrition. There is an increasing incidence of SBS, particularly in premature babies and newborns with congenital intestinal anomalies. Tissue-engineered small intestine (TESI) offers a therapeutic alternative to the current standard treatment, intestinal transplantation, and has the potential to solve its biggest challenges, namely donor shortage and life-long immunosuppression. We have previously demonstrated that TESI can be generated from mouse and human small intestine and histologically replicates key components of native intestine. We hypothesized that TESI also recapitulates native small intestine function. Organoid units were generated from mouse or human donor intestine and implanted into genetically identical or immunodeficient host mice. After 4 wk, TESI was harvested and either fixed and paraffin embedded or immediately subjected to assays to illustrate function. We demonstrated that both mouse and human tissue-engineered small intestine grew into an appropriately polarized sphere of intact epithelium facing a lumen, contiguous with supporting mesenchyme, muscle, and stem/progenitor cells. The epithelium demonstrated major ultrastructural components, including tight junctions and microvilli, transporters, and functional brush-border and digestive enzymes. This study demonstrates that tissue-engineered small intestine possesses a well-differentiated epithelium with intact ion transporters/channels, functional brush-border enzymes, and similar ultrastructural components to native tissue, including progenitor cells, whether derived from mouse or human cells.

Scientific Abstract:
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